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## United States Patent [19]

Wahl et al.

[11] Patent Number:

5,677,177

[45] Date of Patent:

Oct. 14, 1997

[54]	FLP-MEDIATED GENE MODIFICATION IN
	MAMMALIAN CELLS, AND COMPOSITIONS
	AND CELLS USEFUL THEREFOR

[75] Inventors: Geoffrey M. Wahl; Stephen V.

O'Gorman, both of San Diego, Calif.

[73] Assignee: The Salk Institute for Biological

Studies, La Jolla, Calif.

[21] Appl. No.: 486,409

[56]

[22] Filed: Jun. 7, 1995

## Related U.S. Application Data

[62] Division of Ser. No. 147 912, Nov. 3, 1993, which is a continuation of Ser. No. 666,252, Mar. 8, 1991, abandoned.

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Primary Examiner—Christopher S. F. Low Attorney, Agent, or Firm—Gray Cary Ware & Freidenrich; Stephen E. Reiter

## [57] ABSTRACT

A gene activation/inactivation and site-specific integration system has been developed for mammalian cells. The invention system is based on the recombination of transfected sequences by FLP, a recombinase derived from Saccharomyces. In several cell lines, FLP has been shown to rapidly and precisely recombine copies of its specific target sequence. For example, a chromosomally integrated, silent  $\beta$ -galactosidase reporter gene was activated for expression by FLP-mediated removal of intervening sequences to generate clones of marked cells. Alternatively, the reverse reaction can be used to target transfected DNA to specific chromosomal sites. These results demonstrate that FLP can be used, for example, to mosaically activate or inactivate transgenes for a variety of therapeutic purposes, as well as for analysis of vertebriate development.

24 Claims, 3 Drawing Sheets